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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,357	05/09/2002	Bernd Ibscher	0273-0009	1386

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,357	IBSCHER ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,26-40 and 43-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,26-40 and 43-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The RCE dated 7-14-05 is acknowledged.

Claims included in the prosecution are 24, 26-40, and 43-58.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 24, 26-40 and 43-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether the gel in the independent claims is for topical application; this is essential since the compositions contain active agents having pharmaceutical activity as well as cosmetic activity. Vitamins are recited in both categories.

While sorbitol, mannitol, inositol, maltitol are sugar alcohols, glucose, fructose, sucrose, trehalose are not sugar alcohols as recited in claim 27. They are sugars.

It is an ophthalmic gel, it is unclear as to how it can be called as cosmetically acceptable formulation as recited in claim 51. Isn't it a pharmaceutical composition? Similar is the case with nasal, vaginal and anal gels. They are not known to be used for cosmetic purposes in these areas.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 24, 26-40, and 43-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 4021082 cited in the previous action.

As discussed above, DE discloses skin treatment compositions containing liposomal gel. The gels contains a phospholipid, phosphatidylcholine (10 %), alcohol (0.1-20 %), inositol (0.1 to 10 %) and the rest water. The alcohol is either a propylene glycol or glycerin or mixtures thereof. (Note the abstract, page 4, line 56 through page 7, line 34, Examples and claims). DE does not teach all of the claimed ranges for the components. In the absence of showing unexpected results, it is deemed obvious to one of ordinary skill in the art to vary the ratios taught by DE to obtain the best possible results with the guidance provided by DE. DE does not appear to teach the additional amounts of glycerol or ethanol as in instant claims. However, in the absence of showing the criticality, in view of its teachings of the use of mixtures, it is deemed obvious to one of ordinary skill in the art to manipulate the basic teachings of DE to obtain the best possible dissolution of an active agent and to obtain the best possible results. Such a skill is within the skill of the art. DO does not appear to teach the use of buffers. However, since the appropriate pH conditions are desirable to prevent the adverse side effects of a composition on the skin when used topically, it is deemed obvious to one of ordinary skill in the art to use buffers. Although the method of preparation described by DE is by mixing the components together it does not appear to teach the mixing to be done in an inert atmosphere. However, it is within the skill of the art to recognize that

phospholipids are susceptible to oxidation and therefore, the mixing has to be done in an oxygen free atmosphere if the phospholipids are unsaturated.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that DE teaches and claims skin treatment agents containing a bilayer source, salts of organic acids, alcohol, a stabilizer and lipids and that the present invention does not teach the use of salts of organic acids, nor of lipids nor a stabilizer within the asserted meaning of those terms in DE. Furthermore, applicant argues that DE teaches the use of urea and or monosaccharides. This argument is not found to be persuasive since according to DE, the organic acids are skin treatment agents and also appear to modify the skin pH. Instant claims recite alpha-hydroxy acids as optional additives having cosmetic action. With regard to the stabilizing agents argued by applicant, the examiner points out that the reference teaches monosaccharides such as glucose, mannose, galactose, sorbitol and inositol. Applicant claims these compounds as polyhydric alcohol in instant claims. Applicant's arguments that there is no teaching or suggestion that on the basis of DE 40210982, one could raise the phospholipid compositions to amounts well in excess of 10 % up to about 60 % are not persuasive. While there is no motivation to raise the phospholipid content to 60 percent, instant claims recite the lower amounts which is closer to 10 % taught by DE and applicant has not shown any expected results at this lower range. The examiner has already suggested the submission of data showing unexpected results for the upper and lower limits of PL and stabilization effect of compounds falling within the

generic terms, 'pentahydric, hexahydric and sugar alcohols' during the interview held on 5-11-05.

5. Claims 24, 26-40, and 43-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 4021082 cited above in combination with EP 0158 444 cited in the previous action or DE 195 20 659 (cited on page 2 of the specification) or Boni (5,820,848 also cited on page 2 of the specification).

The teachings of DE have been discussed above. What are lacking in the teachings of DE are the explicit teachings of higher amounts of phospholipid and the use of a buffer and the use of an inert atmosphere to prepare the phospholipid formulations.

EP discloses compositions containing 45 % phospholipids (unsaturated lecithin or saturated DPPC), 36 % ethylene glycol or propylene glycol and 0.9 % glucose. EP also teaches the use of phosphate buffer of pH 7.4 and the preparation is done in N2 atmosphere. The drugs taught are insulin. According to EP, the preparations have high drug entrapment ratios (abstract, page 5, lines 2425, page 10, lines 11-22; page 12, lines 18-31; page 13, line 34 through page 14, line 34; Examples, examples 16 and 18 in particular).

The reference of DE (659) teaches compositions containing 5-35 percent of phospholipid. The compositions also contain a mixture of di or trihydric alcohol with ethanol (see page 2 of instant specification).

Boni teaches phospholipid gels containing 99 percent of DPPC. The compositions also contain alcohols such as ethanol and glycerol (abstract, col. 10 and examples, example 2 in particular).

It would have been obvious to one of ordinary skill in the art to increase the amount of the phospholipid in DE with a reasonable expectation of increasing the amount of active agent which is entrapped since EP shows the use of higher amounts of phospholipids and increased amounts of entrapped agent with these higher amounts and both DE and Boni show the routine use of higher amounts of phospholipids in gel formulations. It would have been obvious to one of ordinary skill in the art to use appropriate buffers when used in combination with labile drugs such as insulin and use an inert atmosphere while preparing the compositions as evident from EP and from the guidance provided by EP with a reasonable expectation of success. The use of hydrogenated phosphatidylcholine instead of unsaturated compound, with a reasonable expectation of success, would have been obvious to one of ordinary skill in the art since EP advocates such a use.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments that the deficiencies in DE extend not only to the higher concentration of phospholipid, but to the exclusion of DE's organic acids, lipids and stabilizers have already been addressed by the examiner. Applicant argues that DE and EP are not combinable since DE is directed to skin treatment compositions and EP teaches pro-liposomal compositions comprising phospholipids capable of forming liposomes when agitated in excess water and for use as drug carrier. This argument is

not persuasive. First of all, irrespective of what the formulation is used for, EP deals with liposome preparations and the use of buffers when appropriate and the method of formation of bilayer structures and these will be the same irrespective of the intended use. Secondly, applicant is incorrect in stating that EP is just meant as a drug carrier. EP is meant for both internal and external use as evident from page 9, lines 19-21. Applicant's arguments that while EP teaches the use of water miscible liquid which is a solvent for its membrane lipid, but there is no teaching that the water miscible liquid which is a solvent for its membrane lipid must also contain at least one dihydric or trihydric alcohol and at least one polyhydric alcohol are not persuasive since EP is combined for its teachings of the use of higher amounts of phospholipids. Furthermore, the use of higher amounts of phospholipids is also evident from Boni and DE 659. Applicant provides no arguments regarding these references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK